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# A collaborative robotic solution to partly automate SARS-CoV-2 serological tests in small facilities

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# ABSTRACT

The outbreak of COVID-19 has introduced a significant stress on the healthcare systems of many countries. The availability of quick and reliable screening methodologies can be regarded as the keystone approach to mitigate the spread of the infection until mass vaccination campaigns will be made available to the population. In this scenario, robotics technology can serve as a substantial help in clinical laboratories to speed up the activities.

This work describes in the details a collaborative robotics application developed in partnership with a clinical hospital and a robot manufacturer to partly automate SARS-CoV-2 quantitative serological tests. This technology can be particularly beneficial for small laboratory facilities to alleviate technicians from performing repetitive operations. By automating part of the operations, the overall throughput can be increased of 66%, while the amount of possibly harmful pipetting activities performed by the human can be reduced of 62%.

#### Introduction

In December 2019, China reported first cases of a novel severe respiratory disease in Wuhan (Hubei), caused by a previously unknown pathogen, lately isolated and classified as SARS-CoV-2. The corresponding disease, named COVID-19, rapidly spread in all countries and on March 12, 2020, the World Health Organization (WHO) declared a pandemic situation.

The robotics community has quantitatively contributed to suggest the use of robotic solutions in preventing and fighting the COVID-19 outbreak [1,2]. Several solutions have been proposed, ranging from robotcontrolled for ultraviolet (UV) non-contact surface disinfection, to telepresence robots in hospitals, from social robots for quarantined patients to robots for surveillance and logistics.

When dealing with a pandemic spread and specifically to the one due to SARS- CoV-2, the delay between symptoms onset and isolation plays the largest role in determining whether the outbreak can be controlled or contained [3]. The current situation in many countries shows that the healthcare system quickly reaches its testing capabilities when laboratory capacity is saturated or cannot be converted.

Two well distinct options for robot-based automation of laboratory processes are available. On the one hand, the complete automation (or Total Laboratory Automation, TLA) of the process is certainly a valuable solution [4–6]. The automation takes over completely the role of lab technicians in activities like sample preparation [7], pipetting [8], liquid handling [9,10], and test execution. Alternatively, the robot can carry out only the repetitive activities, while the control of the process remains with the laboratory staff. In the case of partial automation, the

laboratory is retrofitted to introduce robotic solutions e.g., for handling purposes. This can be done very quickly with collaborative robots [11]. Collaborative robots are indeed redefining laboratory automation offering flexible, yet autonomous, workstations designed for various manual tasks in both clinical and basic research laboratories. An interesting debate has recently divided roboticists: those supporting collaborative robotics [12], and those who do not [13]. The main benefit of having humans and robots working together is the augmented throughput and a relatively small effort in the integration of a robotized solution. Technicians working with robots are not necessarily expert in robotics. They just need a very short training on how to start/stop/pause an application, and on how to recovery from errors. This characteristics is intrinsic to all collaborative robotics installations. Interestingly, we have found the same paradigm of manufacturing automation applicable also to lab automation and test facilities: collaborative robotic solutions represent a good compromise between complexity/cost/throughput of hard automation solution and flexibility and adaptability of completely manual implementations [14,15]. In our opinion, solutions based on collaborative anthropomorphic robots are more convenient than alternative ones based on Cartesian or SCARA robots. This happens especially in small facilities, where robots are considered and installed only if able handle different kind of tasks, instead of being tailored to specific applications, like for example pipetting in the case of SCARA robots.

The pandemic outbreak of the COVID-19 might have dramatically changed the perspective. Figure 1 reports the number of daily processed molecular tests for COVID-19 diagnosis in Italy. From an average value of 3 thousand in late February (the beginning of the pandemic spread in Italy), in approximately 2 months, the national throughput has raised

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Fig. 1. Daily (blue) and week average (orange) COVID-19 tests (swabs) in Italy (source: daily statistics from Civil Protection Department, https://www.epicentro. iss.it/coronavirus/open-data/covid\_19-iss.xlsx, accessed June 6, 2021).

of 20 times, until reaching an average of 320 thousand in late March 2021. At the beginning of the outbreak in Northern Italy, only few centralized laboratories were allowed to process molecular test, introducing a substantial delay in the outcome of the tests.

Due to the relatively quick increase in the demand of diagnostic tests, the impact of robots working in the laboratory alongside technicians, as opposed to in monolithic fully automated labs, is significant. A fully automatic laboratory should be designed and built around the robot, requiring a substantial effort in redesigning the protocols, the supply chain of materials and disposables, and typically takes several months. Partial automation solutions, and those adopting collaborative robots, can help in relieving the burden on laboratory personnel at short notice. The robot can take over recurring procedures, thus mitigating the strain on the qualified laboratory personnel. In this case, a collaborative robotic solution is the ideal solution, as it can be used in direct proximity with humans without protective fences, reducing the overall footprint of the laboratory.

This paper describes a collaborative robotic application that consists in the partial automation of quantitative serological tests. Serological tests aim at evaluating a previous exposure to a particular pathogen, the SARS-CoV-2 in this case, by looking for viral-specific antibodies (Ab) in patients' serum. Quantitative tests, additionally, also allow to measure the antibody titer, i.e., its specific amount of antibodies present in serum defined as the inverse of the greatest dilution that still allows to reveal the presence of antibodies. Serological tests, aimed at quantifying the amount of antibodies (title) in the patients' serum are also relevant from different perspectives:

- identify and monitor the stage of the infection in the patient [16];
- support epidemiological screenings on the population.

In addition, the availability of vaccines [17] will inevitably require researchers to monitor the development and the persistence of specific antibodies in vaccinated individuals [18].

In this paper, we refer to quantitative serological tests ELISA (Enzyme-Linked ImmunoSorbent Assay), developed specifically for COVID-19 patients [19], validated at Mount Sinai University, and imported at the European Institute of Oncology (IEO), Milan. The assay has been validated at IEO resulting in 95.2% sensitivity (correct detection) and 97.64% of specificity (correct rejection) for type-g antibodies [20].

The remainder of this work is structured as follows. Section "Why to automate? What to automate?" details the ELISA protocol, its main characteristics and the decision regarding which subtask was worth and convenient to be automated. The design of the application is described in section "Materials and methods". Section "Results and discussion" reports the storyboard of the project and the main issues experienced during the deployment phase. Finally, the last section draws some conclusions.

#### Why to automate? What to automate?

The ELISA procedure consists in the following steps. On day 1, the viral proteins (i.e, either the receptor binding domain (RBD) or the ectodomain of the viral Spike protein, both expressed in mammalian cells) are coated on a microtiter plastic plate and left for overnight incubation at ambient temperature. On day 2, the residual non-coated protein is removed, and the well plate is washed. Then, to avoid aspecific binding, an inert protein is added to the plate, which is left for incubation at room temperature for 60 minutes. The plate is washed again, and the patients' serum is dispensed. During a further incubation period of 90 minutes, if antibodies are present in the serum, they bind to the viral protein. The residual unbound serum is then removed, and the plate is washed again. A secondary antibody, i.e. an anti-human immunoglobulin antibody coupled with the horseradish peroxidase (HRP) enzyme, is added to the wells. If an anti-viral primary antibody is present, the secondary antibody will bind. After 50 additional minutes of incubation, the plate is washed and the substrate of the HRP is added. The role of the substrate is to trigger a colorimetric reaction so to produce a visible signal indicating the presence/quantity of antigen in the sample. After 10 minutes of incubation, the enzymatic reaction is blocked with an acid solution (typically sulphuric acid, H<sub>2</sub>SO<sub>4</sub>) solution, and the assay is ready for being read by measuring the visible absorbance of each well. Figure 2 sketches the main steps of the ELISA test.

In these daily activities in the laboratory, operations are performed manually by lab technicians. For an increased throughput, microtiter plates with 96- or 384-wells and multi-channel micropipettes are typically used. Assuming an 8-channels micropipette is used, and based on the protocol, the pipetting activities is performed 744 times for 96-well plates, and 2976 times for 384-well plates, i.e. approximately 8 times per patient The overall procedure, from when the protein is dispensed to the outcome of the test, takes approximately 13 hours, while the leadtime (from when the serum is dispensed to when the results are ready) is of about 3 hours, and the overall processing time is of 20 minutes of manual work. Each of the four washing cycles takes approximately 3 minutes, constituting the 60% of the processing time. Washings are by



Fig. 2. Main phases of the enzyme-linked immunosorbent assay (ELISA), incubation periods as well as the reading procedure are not represented (please refer to the manuscript for a complete description of the assay).

far the most repetitive activities and constitute the 77% of all pipetting operations.

Prolonged pipetting activities can lead to serious repetitive strain injuries, and especially cumulative trauma disorders (CTDs). These disorders include nerve injuries (such as carpal tunnel syndrome, CTS), joint problems, muscle/tendon disorders. Thumb tenosynovitis, also known as the "Pipettor's Thumb", is probably one of the most common laboratory thumb injuries. As intensively studied in the literature [21], repeatedly depressing a pipette plunger may lead to the overuse of the muscle/tendon compound putting the thumb in the hitch-hiking position, causing this injury.

In view of the discussion above, it should result clear that washing cycles are candidate activities more convenient to automate (a) being repetitive, (b) being more time consuming, and (c) having the highest impact on the musculoskeletal system if performed by the technician. Moreover, differently from other phases of the assay, the washing cycles can be performed without changing the pipette tips, without the risk of cross-contamination. Finally, the way washing cycles are executed (i.e., manually by the technician or by automatically by a robot) is not affecting the performance of the assay in terms of sensitivity and specificity.

In the following we will discuss the adopted strategy to automate the washing procedures. As the introduction of a robotic solution will complement and not substitute human labor, the natural selection will be towards a collaborative robotic solution. Here and in the reminder of the work, the adoption of a 96-well plate is assumed without the lacking in generality. In fact, while the robot is clearly able to operate 384-well plates (its repeatability is of approximately 0.02 mm), difficulties for the operator in dispensing reagents in higher-throughput plates have been reported.

#### Materials and methods

As anticipated, the collaborative robot will be responsible for the 4 washing cycles representing the 66% of the total time, and the 77% of the pipetting actions in case of completely manual execution. Each washing cycle consists in adding and then removing 0.1% tween-20 in phosphate-buffered saline (TPBS) solution for each well and for three times. The solution is taken from a reservoir and dispensed in all the 96 wells. Then, the solution is removed from the wells and disposed in another container. This operation is repeated 3 times within a single washing cycle. Each of the 96 wells of a micro-plate has a circular footprint of 8 mm of diameter, and wells are arranged in 8 rows and 12 columns. This Section details how the tooling and the human-robot synchronization have been designed.

The robot used in this application is the dual-arm ABB YuMi (ABB S.p.A., Milano). The robot has two 7-dof arms and is suitable for use in clean room environments (cleanroom air cleanliness of class 5, according to ISO 14644-1) and can be instructed using the proprietary programming language (ABB RAPID).

The robot was available in the laboratory of Politecnico di Milano and was already adopted in previous experiences for pipetting operations. The main reason for the selection was the availability of the hardware in the lab. On the other hand, we firmly believe in the opportunity of adopting anthropomorphic collaborative robots in place of other robots. A possible limitation of more traditional Cartesian or SCARA liquid handler is surely its limited flexibility. While they are surely suited for liquid handling tasks (including pipetting) and therefore for this application, an anthropomorphic arm can be really adopted in a variety of tasks. For example, the same model of robot has been used for sorting COVID-19 swab samples in another hospital in the Province of Bergamo (near Milano) within the project COVIMATIC (https://covmatic.org). The robot is responsible for reading the bar code attached to the samples and to guarantee the traceability of the qPCR tests. Switching from one application to the other, is a matter of few hours, mainly to change the toolings (robot fingers) and the components (tubes rack and buffers), while from a software point of view it is just a matter of loading the right program onto the system. In this sense, we believe that the robot adopted in this study, though being presented in terms of pipetting, can be reused in other laboratory tasks. Small facilities, which is the target for this application, have no necessity of very high throughput and they may benefit of reallocating the robot based on varying needs. For these reasons, we believe that the solution adopting a collaborative anthropomorphic robot can be of interest also in other applications.

## **End-of-arm toolings**

An 8-channels Rainin Pipet-LiteTM XLS+ micropipette produced by Mettler Toledo (Mettler-Toledo S.p.A., Milano) with volumes in the range 20-300  $\mu$ L has been adopted in this application. The pipette is a standard one for manual pipetting. Therefore the volumes are adjusted by manually rotating the knob.

These kinds of tools are very common in basic research or clinical laboratories. As a piston moves upward, driven by the depression of a plunger, which is manually actuated by the technician, vacuum is created, and the liquid is collected. A return spring allows the piston and the plunger to go back into rest position. The piston-plunger complex has a maximum stroke of 20 mm (corresponding to 300  $\mu$ L) and to be fully compressed exerts a return force of F = 13 N (corresponding to a spring stiffness of 650 N/m). Different technologies for the actuation of the piston-plunger complex of the multi-channel pipette have been compared. A simple electromagnetic solution (solenoid with or without return spring) has been found not adequate for the limited stroke capacity. Mechatronic solutions, consisting in direct-drive or linear servomotors, have been also excluded because of their need for additional hardware (i.e., the driving electronics and the corresponding control). The attention has finally been focused on pneumatic actuation. Doubleeffect pin cylinders have been selected as the candidate technology for the actuation of the piston-plunger complex. The force-pressure-bore characteristics on outstroke is as follows:

$$F = \frac{\pi d^2}{4} \Delta P$$

where d is the bore size,  $\Delta P$  is the operating pressure, and F is the corresponding outstroke force. A commercial SMC CJP2 pin cylinder with stroke 20 mm and bore size of d = 6 mm (SMC Italia S.p.A., Brugherio, Italy) has been selected to operate at pressure  $\Delta P = 0.6$  MPa (corresponding to a nominal outstroke force of F = 17 N). A clamping tool 3D printed in polyamide (SLS, Selective Laser Sintering) has been designed to host the micropipette and to hold the cylinder. A rendering of the tool is shown in Fig. 3(right) as attached to the flange of one arm of the



Fig. 3. The layout of the collaborative application: the dual-arm ABB YuMi robot performing the washing procedures, the two buffers (one occupied), and the two reservoirs. On the left a detailed view of the designed gripper from ABB RobotStudio, while on the right a rendering of the tool consisting of a Rainin 8-channels micropipette and an SMC dual-effect pneumatic pin cylinder (again from ABB RobotStudio).



**Fig. 4.** Pneumatic (top) and electrical (bottom) interfaces and connections to the digital I/O board embedded in the robot controller.

ABB YuMi robot used in this study. The total weight of the tool is of approximately 0.4 kg. The cylinder is actuated through a 5/3-way valve equipped with two spring/solenoid actuators. Solenoids are driven at 24 Vdc by the I/O board embedded within the robot controller. The pneumatic circuit and the corresponding actuation are shown in Fig. 4(top).

As already stated, the robot and the lab technician never work simultaneously on the same micro-plate, but rather one takes over the other during the processing. More in particular, the collaborative workstation (see again Fig. 3 for a rendering obtained during the design process) is equipped with two buffers. One of them serves as a feeding buffer for the technician and will contain a micro-plate ready for the washing procedure, while the other one will contain the processed micro-plate after being washed by the robot. Buffers have been designed with sloped edges to compensate for small misalignments. In addition, two cylindrical pivots have been added to the feeding buffer preventing the technician to deposit the well-plate with the wrong orientation. The right arm of the robot, which is equipped by its off-the-shelf parallel servo gripper (custom fingers have been also made in polyamide), is responsible for the handling of the plates. Specifically designed fingertips have been mounted on the right hand of the robot. The shape of the top finger (see once again Fig. 3(left)) is meant to align to the edge of the plate and provide an additional centering capability. The lower finger, in turn, presents a tooth that aligns with the cavity of the plate and guarantees a stable grasp. An additional station has been positioned in front of the robot to contain the micro-plate currently in process.

## Workflow

Based on the distribution of jobs between the collaborative robot and the technician, the processing has been organized in batches. Each 96-wells plate requires 12 minutes for the robot (to perform 4 washing cycles of 3 minute each) and 8 for the technician (to perform the remaining activities). If performed fully manually, the task requires 20 minutes of human labor, as already mentioned. Therefore, the theoretical maximum throughput of the collaborative workstation is of 5 plates every hour (480 patients), as compared to 3 (288 patients per hour) when performed manually by one technician. Accordingly, the number of pipetting thumb activities demanded to the technicians reduces from 2232 to 840 actions per hour. In relative terms, productivity can be increased of 66%, while the ergonomic effort demanded to the technician is reduced of 62%. Overall, despite the increased throughput in terms of daily processed tests, the time spent by the technician decreases of 33%.

The Gantt chart corresponding to the first micro-plate in the batch is shown in Fig. 5. The remaining micro-plates in the same batch are processed analogously and interleaved so to mask almost completely the incubation periods.

As the workflow of the application suggests, appropriate synchronization systems between the robot and the technician are needed. In particular, the robot must be aware of when a new micro-plate is available in the feeding buffer and whether the drop-off buffer is free or not. The two buffers have been equipped with two 24 Vdc-supplied normally open (NO) switches. The state of the buffers (either empty or not) is read directly by I/O module embedded within the robot controller, see Fig. 4(bottom). Upon the availability of a new micro-plate in the



Fig. 5. Gantt chart for the processing of one 96-wells micro-plate (time in minutes). Activities assigned to the technician are in blue, those to the robots are in cyan. The remaining micro-plates in the same batch are interleaved and processed analogously.



**Fig. 6.** Details of the target positions for the dispensing (black) and for the aspiring (gray) phases, together with the approaching paths for the dispensing (blue), and for the aspiring (red) phases.

feeding buffer, the right arm of the robot picks it up and accommodates it within the processing fixture to start the washing cycle with the left arm. When completed, the right arm check for the state of the drop-off buffer. If free, the robot makes the washed micro-plate available to the lab technician to continue with the process.

During nominal operations, the technician interacts with the robotic station by loading and unloading the micro-plates in the corresponding buffers. In case of errors, the technician is instructed to halt the robot, recover from errors using the build-in lead-through modality, and resume the application using the teach pendant of the robot. A video of the overall application is available at the following link https://www.youtube.com/watch?v=7nSuc3ZIOSA.

The robot has been programmed in the native programming language, i.e., ABB RAPID, first using an offline simulation tool, then directly on the robot primarily for the fine tuning of the grasping positions. A total number of 8 robot target positions, 4 per each arm, have been programmed. In particular, 3 for the right arm are for the feeding, the drop-off, and the working buffers, whilst 3 for the left arm are for the first well of the micro-plate, and the two reservoirs. The remaining 2 are the rest positions, one per each robot. Other robot target points as well as waypoints have been defined relatively to one of the aforementioned positions by considering the relative offsets of 9 mm between wells (see Fig. 6). The reduced number of targets to be specified clearly make this application easily replicable in other labs. Particularly interesting is the definition of the position of the first well of the micro-plate. The dispensing position has been defined, while the aspiration one has been obtained by adding an offset and a tilt angle to the dispensing position (see again Fig. 6). In particular, the offset along the direction of the tips has been selected equal to 9 mm to meet the requirement on the suggested immersion depth for the given volume of 100  $\mu$ L, while a tilt angle of 20 degrees, equivalent to maximum recommended value by the pipette manufacturer, has been introduced with respect to the vertical. According to the manufacturer, such a tilting angle has been proved to guarantee higher performance during the aspiration phase, with respect to a non-tilted orientation of the pipette. As a matter of fact, no significant difference has been noticed. On the other hand, the tilted angle could guarantee a faster movement of the robot.

# **Considerations on safety**

The analysis of safety is surely deserving a detailed discussion. There are two major possible sources of hazards for the human operator. The former is related to the biochemical exposure, the latter refers to moving parts.

As for the biochemical risk for the operator, it is worth noticing that the serum has been proved substantially free of viral load [22], and



Fig. 7. Breakdown of engineering activities: project management (dark blue, 9%), design of tools (orange, 17%), offline programming (grey, 21%), pre-commissioning (yellow, 39%), and fine tuning of parameters (light blue, 13%).

therefore only standard BSL (biosafety level) of 1 or 2 can be implemented, at least for the specific application.

In turn, a particular attention has been paid to the risk of mechanical hazards due to the motion of the robot. As the directives suggest [23,24], there are two types of hazards to consider: one is due to the transfer of kinetic energy from the robot to the operator, the other one is due to the possibility of clamping human's parts with the robot. While the robot is already satisfying all the safety criterion, the specific tool that has been designed is not. Therefore, before the implementation, the actual risks for the technician have been analyzed. It turned out that the sole source of hazard is related to the downward motion of the left arm of the robot (the one holding the micropipette), and the actual source of danger is due to the tips. Having a diameter of 0.75 mm, and assuming a possible clamping (quasi-static contact) with the hand of the technician, the maximum velocity of the robot during this specific phase must be lower than:

$$v^{max} = \frac{p^{max}A}{\sqrt{m_R k_H}} = 1.8 \ mm/s$$

where A is the area of the tip,  $m_R = 2.95$  kg is the equivalent mass of the robot (including the tool),  $k_H = 75$  N/mm is the stiffness of the human hand [24], while  $p^{max} = 190$  N/cm<sup>2</sup> is the maximum permissible pressure for the given body part in quasi-static contact situations [24]. As this velocity significantly limits the throughput of the washing operators, it has been decided to setup an acrylic glass panel for the protection of the technician (see again Fig. 3) against clamping situation with the pipette tips. This panel has been sized to leave free the remaining part of the collaborative workstation for the cooperation of the technician with the other arm of the robot.

# **Results and discussion**

The project has been officially kicked-off on April 3rd, 2020 (while Italy was almost completely in lock-down), and the collaborative workstation has been tested completely on June 12th, 2020. The development phase has progressed quite smoothly, with only one exception. At the beginning of the project, one arm of the robot was indeed assumed capable of pushing against the piston of the micropipette held by the other arm. Under this assumption, a bimanual operation was foreseen to perform both aspiring and dispensing tasks. During the first run of physical experiments at the end of April, the robot was shown not capable of performing the pipetting operation as initially conceived. Despite the vicinity of a singular configuration, the arm holding the pipette was indeed not strong enough to sustain the force of the other arm pressuring on the piston. The holding tool has been re-designed to host the pneumatic cylinder described in the previous Section, playing the role of the technician's thumb. A more evolved digitalized environment would have helped in preventing this erroneous evaluation. In particular, simulator capable of handling at least statics, or even dynamics, would have had a discrete impact in speeding up the design phase.

Figure 7 reports the breakdown of engineering activities, that required approximately 2 weeks of FTE (Full-Time Equivalent) engineering personnel. Approximately half of the work has been spent remotely during the lockdown. Most the RAPID code running on the robot has been preliminary validated in a simulation environment (ABB Robot Studio). In turn, the remaining part of the work, which represents the 52% of the total effort and includes the pre-commissioning phase and the final tuning of the parameters has been spent in the lab of Politecnico di Milano, before the commissioning phase. More in the details, the pre-commissioning phase represents by far the most demanding activity (39%). As a matter of fact, this activity required the physical presence of engineering personnel in the laboratory for the design and the positioning of the fixtures, wire connections, and some workshop activity. In turn, the programming phase, which constitutes no more than the 34% of the engineering effort has been mostly handled using a simulation environment (21%) except for the final fine tuning of the robot positions (13%) that has to be performed in the laboratory. As already discussed in the previous Section, the RAPID program has been structured so that only 8 targets (4 per each arm) have to be specified. It follows that the reprogramming effort in replicating this application in another lab is reduced to one working day or even less. This fact is also due to the simplification in robot programming of this new generation of robotic platforms that allows non-experts to teach new positions by simply manually dragging the robot to the target (such a modality is called free-drive or lead through teaching).

Still referring to Fig. 1, it is worth noticing that after the peak of daily tests in the second half of May 2020, as of July 2020 the number of daily processed swabs has been decreased of the 33%. In turn, the beginning of the second wave, in Autumn 2020, has significantly increased the number of daily processed tests, which is more than doubled with respect to Spring, before decreased again in January 2021. As it is happening in manufacturing companies with the fluctuation of the market demand, also in the case of COVID-19 tests a non-constant operability has been reported. Therefore, the flexibility of the automation solution, that only collaborative robotics applications can guarantee, is of paramount importance. The possibility to quickly redeploy or adapt an application to respond to other needs can be only guaranteed with the adoption of robots, rather than hard automation solution. For these reasons, this collaborative robotics solution can be particularly beneficial for small research infrastructures, in the laboratories of small or field hospitals, or ultimately as an as-a-service solution for residential cares, private companies, etc.

# Conclusions

This paper described a collaborative robotic operation for the partial automation of the processing of quantitative serological tests for SARS-CoV-2 antibodies. A dual-arm robot manipulator has been programmed to automate the washing phases of the serological assay which constitute two thirds of the processing time. Among the others, this specific activity has been considered the most susceptible of automation being repetitive, time consuming, and potentially of high impact on the musculoskeletal system of the technician. The overall solution guarantees a processing capability of 480 tests per hour, as compared to 288 when performed by the technician only (+66%), as well as a reduced ergonomic effort for the technician from 2232 to 840 pipetting actions per hour (62%), despite the increased processing capability. The design of the application has been described together with all relevant details, for being replicated elsewhere in case of need.

Clearly, in terms of throughput the proposed solution cannot compete neither with fully automated ones, nor with ones based on tailored hardware for pipetting. In turn, the main advantage of collaborative robotics is the ease of use and their extreme flexibility. Next studies are planned to prove the adaptability of these robots to other laboratory tasks.

## **Declaration of Competing Interest**

The authors declare no conflict of interest with respect to the research, authorship, and publication of this article.

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#### References

- Yang G, Guang-Zhong, et al. Combating COVID-19—The role of robotics in managing public health and infectious diseases. Sci Robot 2020.
- [2] Shen Yang, et al. Robots under COVID-19 pandemic: A comprehensive survey. IEEE Access; 2020.

- [3] Hellewell Joel, et al. Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. Lancet Global Health 2020:488–96.
- [4] Boyd J. Robotic laboratory automation. Science 2002;295:517-18.
- [5] Chapman T. Lab automation and robotics: Automation on the move. Nature 2003;421:661–3.
- [6] Blow N. Lab automation: tales along the road to automation. Nat Methods 2008;5:109–12.
- [7] Fleischer H, Drews RR, Janson J, et al. Application of a dual-arm robot in complex sample preparation and measurement processes. J Lab Autom 2016;21:671–81.
- [8] Barthels F, Barthels U, Schwickert M, et al. FINDUS: an open-source 3d printable liquid-handling workstation for laboratory automation in life sciences. SLAS Technol 2020;25:190–9.
- [9] Moriello L, Biagiotti L, Melchiorri C, et al. Control of liquid han- dling robotic systems: A feed-forward approach to suppress sloshing. In: IEEE International Conference on Robotics and Automation (ICRA); 2017. p. 4286–91.
- [10] Maderna R, Casalino A, Zanchettin AM, et al. Robotic handling of liquids with spilling avoidance: a constraint-based control approach. In: IEEE International Conference on Robotics and Automation (ICRA); 2018. p. 7414–20.
- [11] Zanchettin AM, Croft E, Ding H, Li M. Collaborative robots in the workplace [from the guest editors]. IEEE Robot Autom Mag 2018;25:16–17.
- [12] Dutton G. Life sciences labs need cobots, not robots: Highres biosolutions modularizes lab automation and favors collaborative robotics. Genetic Eng Biotechnol News 2018;38:8–9.
- [13] McClymont DW, Freemont PS. With all due respect to maholo, lab automation isn't anthropomorphic. Nat Biotechnol 2017;35:312–14.
- [14] Galin R, Meshcheryakov R. Automation and robotics in the context of Industry 4.0: the shift to collaborative robots. IOP Conf Ser: Mater Sci Eng 2019;537:1–5.
- [15] L. Gualtieri, I. Palomba, E.J. Wehrle, R. Vidoni, The opportunities and challenges of SME manufacturing automation: safety and ergonomics in human–robot collaboration. Industry 4.0 for SMEs, 2020, 105-144.
- [16] Bruni M, Cecatiello V, Diaz-Basabe A, et al. Persistence of anti-sars-cov-2 antibodies in non-hospitalized covid-19 convalescent health care workers. J Clin Med 2020;9.
- [17] Kaur SP, Gupta V. Covid-19 vaccine: A comprehensive status report. Virus Res 2020.[18] Widge AT, Rouphael NG, Jackson LA, et al. Durability of responses after sars-cov-2
- mrna-1273 vaccination. N Engl J Med 2021. [19] Amanat F, Stadlbauer D, Strohmeier S, et al. A serological assay to detect sars-cov-2
- seroconversion in humans. Nat Med 2020.
- [20] Valenti L, Bergna A, Pelusi S, et al. Sars-cov-2 seroprevalence trends in healthy blood donors during the covid-19 outbreak in milan. Blood Transfusion 2021;19.
- [21] Wu JZ, Sinsel EW, Shroyer JF, et al. Analysis of the musculoskeletal loading of the thumb during pipetting-a pilot study. J Biomech 2014;47:392–9.
- [22] Kim J-M, Kim HM, Lee EJ, et al. Detection and isolation of sars-cov-2 in serum, urine, and stool specimens of covid-19 patients from the republic of korea. Osong Public Health Res Perspect 2020;11.
- [23] Rossi R, Polverini MP, Zanchettin AM, et al. A pre-collision control strategy for human-robot interaction based on dissipated energy in potential inelastic impacts IEEE/RSJ International Conference on Intelligent Robots and Systems (IROS); 2015.
- [24] ISO TC184/SC2, ISO/TS 15066 Robots and robotic devices Safety requirements for industrial robots – Collaborative operation, 2013.